inconsistent. Stated differently, the fact that a claim may be broad such that it encompasses several embodiments is not a basis to reject that claim as indefinite. *In re Skoll*, 187 U.S.P.Q. 481 (C.C.P.A. 1975)(claim reciting organic and inorganic acids found to be broad, not indefinite).

This argument, which was fully made in the previous amendment is the response to the Examiner's rejection because the Examiner has failed to make a rejection that complies with legal requirements. Nevertheless, the claims state that the linker is bonded to the binding moieties. Nothing in this claims supports the Examiner's suggestions that the claims might be limited to binding in identical positions, although persons skilled in the art will appreciate that some positions are far more easily modified than others. The Examiner has not explained why a person skilled in the art would be unable to understand the scope of the claims, and has therefore failed to make out a sustainable rejection under 35 USC § 112, second paragraph.

The Examiner has also asserted that the claims are indefinite because the "nature of the linker is not known." Again, the Examiner has provided no reasoning why a person skilled in the art, having read the specification, would have any doubt as to whether there is a linker (that is something between the geldanamycins) in a given species, and has therefore failed to make out a sustainable rejection under 35 USC § 112, second paragraph.

With respect to claims 12 and 26-30, the Examiner incorrectly asserts that Applicants have not responded to the prior rejection asserting that these claims are indefinite because "it is unclear where the cells are destroyed." The previous response stated that

> With respect to the Examiner's remarks concerning claims 12 and 26-30 in which he implies that destroying cells in a petri would not accomplish anything (thus raising a specter of a utility rejection), Applicants point out that destroying cancerous cells *ex vivo* (including in a petri dish) may be desirable where material is removed from a patient, treated and later returned.

In short, the claims mean exactly what they say -- destroying cells. If cells are destroyed, the claim does not distinguish between locations where this is accomplished. As to the Examiner's assertion that "it is unclear which cells are expressing a HER-family tyrosine kinase and which ones are not", this assertion is not understood by Applicants. Claim is directed to destroying cells that do express the HER-family kinase. To the extent that other cells are present, they are not relevant to the claimed method.

The Examiner has also rejected method claims 13-17 and 31-36 under 35 USC § 112, first paragraph. Applicants fully anticipate that this issue will need to be addressed on appeal. However, it is noted that the Examiner has refused to even comment on the evidence submitted in this case concerning the generally utility of a monomeric ansamycin compound, 17-allylamino-geldanamycin (17-AAG), which is mentioned in the specification on Page 8, line 15 and other hsp90 inhibitors are efficacious in a variety of tumor types including breast cancer, ovarian cancer, pancreatic cancer and gastric cancer (the cancer types specifically mentioned on Page 8, lines 9-11 of the application), other HER kinase overexpressing tumors, and tumors which do not over express HER kinase. For example, Yang et al. (Exhibit A), report inhibition of glioma (brain tumor) cells with 17-AAG. Okabe et al. (Exhibit B) reports *in vivo* activity of herbimycin A (an ansamycin antibiotic) against leukemia cells. Kelland *et al* (Exhibit C, JNCI 91: 1940, 1999) achieved tumor cytostasis in two human colorectal carcinomas, HT29 and BE for the duration of drug treatment with 17-AAG. Burger *et al* (Exhibit D Proc. AACR, 41: Abstract # 2844, 2000) reported potent effects of 17-AAG against a melanoma xenograft and, interestingly, preliminary data from the London arm of the 17-AAG trial indicates that melanoma (2/6 objective responses) may be a responsive tumor (Exhibit E Banerji *et al*, Proc. ASCO, Abstract # 326, 2001) 17-AAG has also been used in studies with prostate cancers, and it has been shown that this administration resulted in dose-dependent inhibition of androgen-dependent and -independent prostate cancer xenografts. (Exhibit F Solit et al., *Clin. Cancer Res.* 8: 986-993, 2002). 17-AAG has also been shown to enhance paclitaxel-mediated cytotoxicity in lung cancer cells (Exhibit G Nguyen et al, *Ann. Thorac. Surg.* 72: 371-379, 2001); and to modulate

metastasis phenotypes in non-small cell lung cancer (Exhibit H Nguyen et al., *Ann. Thorac. Surg.* 70: 1853-60, 2000). These documents show that the efficacy of compounds that bind to the hsp90 receptor span a wide range of unrelated cancers, thereby refuting the Examiner's statement that generalized cancer therapy is inherently unbelievable. If the rejection is not withdrawn, the Examiner is requested to provide some meaningful commentary concerning these articles, so that the record is complete for appeal.

Finally, Applicants are puzzled by the Examiner's assertion that "Applicants' reliance on the Brana decision is erroneous" since Brana has not been cited by Applicants in this case. However, since the Examiner raised the issue, Applicants will address *Brana* here.

In re Brana, 34 USPQ2d 1436 (Fed. Cir. 1995) was cited in the parent case, and as noted there, compositions which were said to have "anti-tumor activity" were found in *Brana* to meet the enablement/utility requirement because there were examples in specific tumor models which corresponded to specific diseases. Here, specific cancer types are named (and claimed in method claims 31-34). The Examiner says that this case is not controlling because (1) "the compounds on appeal were of much narrower scope"; (2) there were no method claims; (3) the compounds on appeal "were similar in structure to compounds displaying *in vivo* tumor activity." Applicants submit that these three distinctions are not supported by a consideration of the Brana case and the present application.

The assertion that the Brana compounds were of narrower scope has not been explained by the Examiner. The Brana compound has 4 variable substituents, each of which can be independently selected from a long list of possible combinations. There is no meaningful distinction between this claim and those of the present application in terms of the number of compounds, since the number is each case is large.

The comment that Brana is inapplicable because there were no method claims ignores that holding in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971) (which was cited in this case but not mentioned by the Examiner), where it is noted that:

> a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond to those used in

> describing and defining the subject matter sought to be patents *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112, *unless* there is a reason to doubt the objective truth of the statements contained therein, which must be relied upon for an enabling disclosure.

It also ignores the evidence submitted upon which the Examiner has not commented. Furthermore, it seeks to apply a case for what it does not say, when the reason nothing was said was that the issue was not before the court. This is improper.

Finally, the evidence submitted in the last response establishes that the compounds in this case bear structural similarity to compounds having tumor activity. Thus, this distinction which the Examiner has asserted exists between the instant claims and Brana is also without merit.

For the foregoing reasons, Applicants submit that the current claims are in form for allowance. Favorable reconsideration and allowance of all claims are respectfully urged.

Respectfully submitted,

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